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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
| 08/704,159 | 08/28/96 | WILLIAMS | J OPHD-02304 |

HM22/0913

EXAMINER

LI, B

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| ART UNIT | PAPER NUMBER |
| 1648 | 31 |

DATE MAILED: 09/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

| | | |
|------------------------------|------------------------|---------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 08/704,159 | WILLIAMS ET AL. |
| | Examiner | Art Unit |
| | Bao Qun Li | 1648 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 25 July 2001.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) 44,45,58-63,84,85,87,88,95-99 and 102 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) _____ is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) 42-43, 54-57, 79-80, 83, 89-91, 93-94, 100, 103-105 and 107-109 are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____

- 4) Interview Summary (PTO-413) Paper No(s). _____
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____

U.S. Patent and Trademark Office
PTO-326 (Rev. 04-01)

Office Action Summary

Part of Paper No. 31

Continuation of Disposition of Claims: Claims pending in the application are 42-45, 54-65 and 79-109 in the scope of the clostridium botulinum type A toxin.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I of claims 42-45, 54-65 and 79-109 and further directed to the Clostrium botulinum type A in Paper No. 29 is acknowledged. The traversal is on the ground(s) that it would be a serious burden for examining all vaccines made from different species of the C botulinum toxin. This is not found persuasive because each type of C botulinum toxin has different structure. It constitutes a serious burden for the Office to search structurally different proteins both in house and in commercial database. Applicants are also reminded that this is not the species election based on the previous office action on paper No. 27 because different sub-groups of the invention (i) -(xxv) are drawn to the structurally different proteins and they also exhibit different immune response.

The requirement is still deemed proper and is therefore made FINAL.

Because the election is made on the scope of the Clostrium botulinum type A to be examined on the merit, any other subgroups of invention, which do not belong to the elected Clostrium botulinum type A, such as Clostrium botulinum type B-G, will not be examined. Therefore, Applicants are reminded to amend the claims to the scope of the elected Clostrium botulinum type A, and cancel other claims that are directed to the other types of the Clostrium botulinum that include the claims 44-45, 58-63, 81-82, 84-85, 87-88, 95-99, 101-102 along with other non-elected claims 46-53 and 66-78 to the non-elected group.

Hence, only claims 42-43, 54-57, 79-80, 83, 86, 89-91, 93-94, 100, 103-105 and 107-109 are considered before the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42, 54-55, 79-80, 93-94 and 107-109 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 42, 54-55, 79-80, 93-94 and 107-109 are indefinite in that the metes and bonds of the portion of Clostridium botulinum toxin type A are not defined. Furthermore, the word of "comprising" used in the claimed invention are relatively word that fails to define what is the structure of the claimed fusion protein molecule. The Clostridium botulinum toxin type A protein is 1296 amino acids in length, are 10 amino acids a portion of the Clostridium botulinum toxin type A or 50 amino acids a portion of the Clostridium botulinum toxin type A in the said claims? Therefore, the claims render indefinite.

Claim 97 is indefinite for reciting "comprising at least a portion of" because it is unclear how much of the Clostridium peptide is required for the reason state supra.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefore ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 42, 54-55, 79-80, 93-94 and 107-109 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-10 of prior U.S. Patent No. 5,919,665. This is a double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 42-43, 54-57, 79-80, 83, 86, 89-91, 93-94, 100, 103-105 and 107-109 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al. (Eur. J. Biochem. 1990, Vol. 189, pp. 73-81), Dobeli et al. (US Patent No. 5,310,663) and Ford et al. (Protein Expression and purification 1991, Vol. 2, pp. 95-107).

The claimed invention are drawn to a recombinant clostridium botulinum type A toxin comprising a portion of Clostridium botulinum type A toxin sequence of C-fragment of the receptor binding site of C botulinum type A toxin and it is fused with the a polyhistidine tag for purification of the said recombinant protein.

Thompson et al. teach the entire amino acid sequence of the C botulinum type A neurotoxin (BoNT/A) deduced by nucleotide sequences analysis of the encoding gene (Figure 3). Thompson et al. Teach that the light chain has the pharmaceutical activity (page 73, Column 1). Thompson et al. teach that the increased use of neurotoxins in the food industry, in neurobiological research, and in clinical user, requires immunization of personnel. Thompson et al. also teach that the viability of the BoNT/A gene sequence will allow the production toxin and toxoid for the formulation of improved vaccines (page 83, last paragraph). Thompson et al. in particular, teach the association of receptor binding properties with the C-terminal portion of the heavy chain (page 73).

Thompson et al. do not teach a recombinant fusion protein comprising a toxin portion of C botulinum type A toxin fused with a polyhistidine tag.

However, there are many well-established methods for making a fusion tails for the recovery and purification of any recombinant protein in the art as evidenced by Ford et al. (Protein Expression and Purification 1991, Vol. 2, pp. 95-107 or Dobeli et al. (US Patent No. 5,310,663). As the detail sequence of the C-fragment of C botulinum type A toxin has been disclosed by Thompson and the detail method for making the poly(His) Tail is further disclosed by Dobeli et al (US Patent No. 5,310,663), the choice of poly(His) Tail to fused with well characterized portion of the C-fragment comprising the receptor binding site of C botulinum type A toxin is just different design choice for the large scale production and purification of the said recombinant C botulinum type A toxin.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references and to combine the teaching

disclosed by Thompson et al. Ford et al or Dobeli et al to make a recombinant Clostridium botulinum type A toxin fused with polyhistidine for the convenient large-scale of the recombinant protein production and purification and then to use the recombinant protein for generate antibody or immune response to meet the large demand of food industry and clinical usage without unexpected results. Hence, the claimed invention as a whole is *prima facie* obvious absence unexpected results.

Conclusion

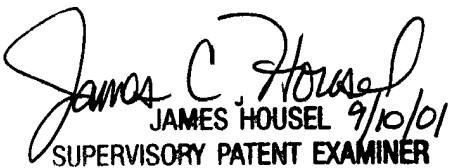
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li
September 4, 2001


JAMES C. HOUSEL 9/10/01
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600